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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,925	12/18/2001	Robert Charles Ladner	DYAX/004	6828

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FISH & NEAVE IP GROUP
ROPES & GRAY LLP
1251 AVENUE OF THE AMERICAS FL C3
NEW YORK, NY 10020-1105

EXAMINER	
PONNALURI, PADMASHRI	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/026,925	LADNER, ROBERT CHARLES	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *1-20,22-41 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21 and 42* is/are rejected.

7)☒ Claim(s) *21 and 42* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed on 8/8/05 has been fully considered and entered into the application.

Applicants response confirms that the elected sequence of CDR3: SEQ ID NO: 8, in which 1 is glycine (G) and 2 is Lysine (K).

2. Applicant's election of group 50 in the reply filed on 4/27/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. It has been NOTED that applicants response filed on 4/27/05, failed to address election of one single combination of light chain CDR (from 1 through 7) from the claim 21. Claim 21 recites that the 'focused library of claim 19, or 20 further **comprising variegated DNA sequence that encodes a light chain CDR selected from the group consisting of** .....' with 7 different combinations.

For compact prosecution applicants response is considered as election of 'focused library comprising variegated DNA sequences that encode all the heavy chain CDR combinations and light chain CDR combinations (from 1-7 of claim 21)'. However, the claims 21 and 42 read on different combinations, applicants are requested to amend the claim to recite '....a focused library of vectors comprising ..... variegated DNA sequence that encodes a) a heavy chain CDR1...., b) heavy chain CDR2...., c) heavy chain CDR3..., d) kappa light chain CDR1..., e) kappa light chain CDR2....., f) kappa light chain CDR3....g) lambda light chain CDR1.....h) lambda light chain CDR2....i) lambda light chain CDR3...' Thus the claim reads on focused

library of variegated DNA sequences that encode all the light chain CDRs, and heavy chain CDRs.

4. Applicant's election with traverse of "kappa light chain CDR1 (SEQ ID NO:14), kappa light chain CDR2 (XASXRXX), kappa light chain CDR3 (SEQ ID NO: 16), lambda light chain CDR1 (SEQ ID NO: 18), lambda light chain CDR2 (XXXXRPS), lambda light chain CDR3 (SEQ ID NO: 19), heavy chain CDR1 (XYXMX), heavy chain CDR2 (AYP), and heavy chain CDR3 (SEQ I DNO: 8)" in the reply filed on 4/27/05 is acknowledged. The traversal is on the ground(s) that 'applicants argue that it is inherent in Applicant's teachings that both the library and the population of variegated DNA sequences comprise diversity of sequences. ... Typically each member of the library differs from the other members of the family having different amino acids or variegation at a given position in the peptide or polypeptide or protein chain. An election of single amino acid sequence for each of the recited CDRs seems to be counter-intuitive to a claim to a library of various sequences.

This is not found persuasive because the instant claims are drawn to library of vectors or genetic packages that display a member of a diverse family of human antibody related polypeptides. Applicant's claims are drawn to various combinations of heavy chain and light chain sequences; and with different core structures for each CDR in heavy chain and light chain. Even if applicants elect one single core structure (i.e., SEQ ID NO: 1 for heavy chain CDR1), the sequence has so much diversity or variegation, which would result in libraries of sequences. Thus, applicant's arguments are not persuasive.

However, Examiner has agreed to consider applicant's election of species of one single amino acid sequence for each of the CDRs in heavy chain or light chain. The elected specific amino acid sequences for each CDR is considered as species election.

The core structure of the elected amino acid sequences is considered as core structure representing the elected group. For example the instant claim 21 is dependent on claim 19, which in turn depends on claim 1 and claim 1 is divided into multiple groups based on specific core structure of heavy chain CDR1. That is the elected core structure of heavy chain CDR1 is XYXMX, heavy chain CDR2 core structure is XIXXSGGXTXYADSVKG, heavy chain CDR3 is YYCAXXXXXXXYFDYWG, kappa light chain CDR1 is RASQXVXXXLA, kappa light chain CDR2 is XASXRXX, kappa light chain CDR3 is QQXXXXPXT, lambda light chain CDR1 is TGXSSXVGXXXXVS, lambda light chain CDR2 is XXXXRPS, lambda light chain CDR3 is XSYXXSXXXV.

The claims 21 and 42 are searched only to the extent of the elected core structure in this application.

5. Applicants in the response filed on 4/27/05 state that the elected group 50 (claim 21 and 42) would read on pending claims 1-42.

This is not persuasive, since the elected group 50 contains only claims 21 and 42. Even though the claims 21 and 42 are dependent on several claims, i.e., claim 19, which in turn dependent on claim 1. Claim 1 is divided into multiple groups based on the core structure of the heavy chain CDR. The elected group claim 21 requires only a single heavy chain CDR1 of claim 1, and does not require the entire claim 1 to be grouped with the elected claim. Claim 21 is searched and examined in this application only to the extent of the elected core structures of the

both heavy chain and light chain CDR. In response to this office action applicants are requested to amend the claim 21 to include the limitations of independent claims.

6. Claims 1-20, 22-41 and 43, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/27/05.

Priority

7. This application claims priority to provisional application 60/256,380 filed on 12/18/00.

Claim Objections

8. Claims 21 and 42 are objected to under 37 CFR 1.75(c) as being in improper form because the claims are dependent on multiple dependent claims 19 or 40. See MPEP § 608.01(n). Accordingly, the claims 21 and 42 not been further treated on the merits.

9. The elected claims 21 and 42 are further dependent on the non-elected with drawn claims. Applicants are requested to amend the claims to include all the limitations of claims 19 and 40.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim Rejections - 35 USC § 101

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 21 and 42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The instant claims briefly recite a 'focused library of vectors comprising variegated DNA sequences that encode a heavy chain CDRs, and light chain CDRs, and the vectors display or express a member of diverse family of human antibody related peptides.' And claim 42 recites a population of variegated DNA that encode light chain CDRs and heavy chain CDRs, and the claim does not recite that the claimed DNA encodes any peptide or not.

According to the text of 35 USC sec. 101, an invention must be useful. Our reviewing courts have applied the labels, specific utility (or practical utility) to refer to this aspect of the useful invention requirement of sec. 101. (Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881, 883 (CCPA 1980)). In Nelson, the court characterized **specific utility (or practical utility)** as a shorthand way of attributing real-world value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner, which provides some immediate benefit to the public. (Id. at 856.)
It thus is clear that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research.

To satisfy the "substantial" utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public. The "specific" utility requirement, an application must disclose a use which is not so vague as to be meaningless, and "that the nebulous expressions 'biological activity' or

'biological properties' appearing in the specification convey no more explicit indication of the usefulness of the compounds. In addition to providing a "substantial" utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public. *See In re Fisher In re Dane K. Fisher and Raghunath V. Lalgudi (CAFC, 04-1465, 9/7/2005).*

According to the PTO Utility Guidelines, 'a specific utility is particular to the subject matter claimed and would not be applicable to a broad class of invention,' and 'utilities that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use or not substantial utilities.'

The 'focused library of vectors or genetic packages that display, display and express a member of a diverse family of human antibody related peptide, or a portion of antibody family' claimed in the instant claims are not supported by a specific, substantial, asserted utility and do not, without further research and experimentation, provide an immediate benefit to the public. The specification disclosure is drawn to methods of making focused libraries of variegated DNA sequences encoding diverse family of human antibody related peptides. The specification has not disclosed a single family of human polypeptides encoded by the claimed library of variegated DNA sequences. The specification has not disclosed the antibody related peptides encoded by the claimed variegated DNA sequences. The specification has not disclosed the screening methods in which the claimed library of DNA Sequences are used.

The specification discloses that the 'Antibodies concentrate their diversity into those regions that are involved in determining affinity and specificity of Ab for particular targets. These regions may be diverse in sequence and length. ....however, within families of human

antibodies diversities, both in sequence and length are not random. Rather, some amino acid residues are preferred at certain positions of CDR and some CDR lengths are preferred.....' However, the specification has not disclosed any one single family of natural antibodies, which are encoded by the claimed library sequences.

The specification has not disclosed any of the DNA sequences encode a specific antibody related peptide. The specification discloses that 'the libraries have length and sequence diversities **that mimic that found** in native human antibodies (see the abstract). However, the specification has not disclosed which natural human antibody the sequences mimic. Applicants focused libraries of variegated DNA sequences seem to be non-specific in function (mimic any native human antibodies), thus the invention lacks specific and substantial utility.

In the absence of specific teachings in the specification which peptides are considered as human antibody related peptides, it is considered that the 'antibody related peptides' may read on orphan receptors, which are known to have known function.

However, the specification neither teaches the 'antibody related peptides', nor the structure and/or function of the 'antibody related peptides' or the relationship of these antibody related peptides to any specific diseases or establish any involvement in the etiology of any specific diseases. Further, the antibody related peptides may read on several unrelated peptides. Therefore the asserted utilities are not considered as "specific utility."

The specification has not disclosed any other asserted utility of the claimed focused vectors comprising variegated DNA sequences.

This is not to say that inventions that are to be used exclusively in a research setting (i.e., research tools) always lack a specific asserted utility. Indeed, many research tools such as

telescopes, gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility. (See USPTO Utility Guidelines.)

However, inventions that have a specifically identified utility must be distinguished from those whose utility requires further research to identify or reasonably confirm. Research tools (such as gas chromatographs, screening assays, etc.) are useful in the sense that they can be used in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result. The claimed focused vectors comprising variegated DNA sequences encoding a member of diverse family of human antibody related peptides' are not research tools in this sense. Rather, they are themselves the subject of basic research (requires to be screened to identify sequences which encode specific antibody related peptides), whose usefulness or lack thereof has yet to be established.

In the absence of an **asserted specific utility**, the useful requirement may be established by reference to a well-established utility. A well established utility is a specific utility which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

The claimed 'focused vectors comprising variegated DNA sequences encoding a member of diverse family of human antibody **related** peptides' are not supported by a well established utility, because it is not known which **antibody related peptide** is encoded by the claimed library of vectors comprising variegated DNA sequences. In the absence of specific disclosure or a definition of which peptides are considered as 'antibody related peptides', no well-established utility can be determined.

However, because neither the specification as filed nor any art of record discloses or suggests any property or activity for the claimed library such that another non-asserted utility would be well established for the compounds.

Note, just because the claims recite that the 'DNA sequences encode a member of diverse family of human antibody related peptides' does not mean that the compounds have substantial utility. In the absence of any data as to their structure and activity, there is no basis upon which to base either a specific or a well-established utility.

Claims 21 and 42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

13. Claims 21 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a lack of written description rejection.

The instant claims briefly recite a 'focused library of vectors comprising variegated DNA sequences that encode a heavy chain CDRs, and light chain CDRs, and the vectors display or express a member of diverse family of human antibody related peptides.' And claim 42 recites a

population of variegated DNA that encode light chain CDRs and heavy chain CDRs, and the claim do not recite that the claimed DNA encodes any peptide or not.

Vas-Cathy Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention."

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

The specification discloses various possible variations of combinations of CDRs of human antibodies. The specification discloses the diversity in the disclosed libraries is generated using different lengths in the CDRs. The specification teaches that the prior art libraries of genetic packages are not focused on naturally occurring diversity and thus no members that are most likely to be functional. However, the specification has not disclosed how the diversity in the claimed libraries is generated.

The specification has not disclosed any of the members of the focused libraries or libraries of variegated DNA sequences encode a specific human antibody related proteins. The

specification has neither disclosed any of the antibody related polypeptides, nor disclosed the definition of the antibody related polypeptides. The specification does not disclose the structure and/or function of the 'antibody related peptides' or the relationship of these antibody related peptides to any specific diseases or establish any involvement in the etiology of any specific diseases.

The specification disclosure if prophetic and has not disclosed any of the single DNA sequence from the claimed library encode a human antibody polypeptide. The specification disclosure is based on hypothetical method, in which diversity or variegation in the amino acid sequence of heavy chain and light chain CDRs are introduced, however, the specification has not disclosed any of these variegated sequences encode a specific family antibody polypeptide.

In absence of any working examples in the specification, the invention lacks written description for the claimed 'focused library of vectors comprising DNA sequences which encode members of human antibody related proteins.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

15. Claims 21 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is dependent on claim 19, which in turn is dependent on claim 1. Thus claim 1 limitations are included in the current claim 21. Claim 1 recites 'a focused library of vectors or genetic packages that display, display and express or comprise a member of diverse family of

human antibody related peptides..... and collectively display, display and express or comprise.....'

The metes and bounds of the terms 'focused', 'antibody related peptides' are not defined in the specification. It is not clear which libraries would infringe the 'focused library' of the instant claims. The specification has not included a definition of the 'focused library.'

The term 'antibody related peptides' is vague and indefinite. The specification has not defined which peptides are considered as antibody related peptides. Does applicants mean blood proteins, or glycopeptides. Does applicants mean that these antibody related peptides are 'structurally related' or functionally related to the antibodies. The specification has neither disclosed the antibody related peptides or which peptides can be selected as antibody related peptides.

The claim recites 'that display, display and express or comprise a member of diverse family of human antibody related peptides', which is vague and indefinite. It is not clear whether the instant claims are drawn to expression libraries or just the vectors comprising the peptides (absence of the DNA). Applicants are requested to amend the claim to clarify.

Allowable Subject Matter

16. The focused library and population of DNA sequences comprising the elected combinations of CDR sequences is free of prior art.

Conclusion

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Primary Examiner
Art Unit 1639

20 October 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER